

REMARKS

Claims 1-3, 5-13, 15-18 and 26 are pending in the application upon grant of the Request for Continued Examination. Claims 1, 11, 18 and 26 are the only claims in independent form. Withdrawal of the previous rejection of claims 1-3, 5-13 and 15-18 under 35 U.S.C. §112, first paragraph is noted with appreciation. Claims 1-3, 5-13, 15-18 and 26 remain rejected under 35 U.S.C. §103(a) over Aebischer et al. Additionally, Claims 1-3, 5-13, 15-18 and 26 remain rejected under 35 U.S.C. §103(a) over Bergmann.

The basis for the outstanding rejections is summarized in section 13 of the Advisory Action (Paper no. 01202006).

Applicant requests reconsideration as to the obviousness of the pending claims on the basis that:

- the claimed invention overcomes the principal cause of side effects associated with progabide by delivering a metabolite thereof (GABAmide) without the aromatic by product 4-chlorophenyl-5-fluoro-2-hydroxyphenylmethanone;
- GABAmide is sufficiently stable as to be amenable to intrathecal and intraventricular delivery; and
- GABAmide is not taught to act like progabide, SL75012 (sodium salt metabolite of progabide), or GABA at all known GABA receptor binding sites.

Applicant submits that neither Aebischer et al. nor Bergmann teaches administration of GABAmide even though it is known as rapidly formed metabolite thereof. Applicant readily concedes that GABAmide is formed in vivo after administration of progabide via oxidative deamination and/or transamination (Bergmann, pg.14, first full para). However, the unexpected reduction in side effects associated with GABAmide administration relative to progabide and

stability of GABAmide to allow intracerebral delivery are believed to be entitled to patentable weight.

The courts have held that when an intermediate is being claimed, identification of the unexpected property and the establishment of a nexus between the claimed intermediate and the result are sufficient to overcome an obviousness rejection.

In *In re Magerlein* (CCPA) 202 USPQ 473, at 479 the court stated:

In order to establish that the claimed intermediate is the "contributing cause" of the unexpectedly superior activity or property of the end product, an applicant must identify the cause of the unexpectedly superior activity or property (compared to the prior art) in the end product and establish a nexus for that cause between the intermediate and the end product.

Applying the holding of *In re Magerlein* to the pending claims, the reduction of side effects associated with progabide by administration of its metabolite, GABAmide and the discovery that GABAmide is sufficiently stable for intrathecal or intraventricular delivery are submitted to be unexpected results over the prior art of record. The reduction of side effects directly tied to the claimed administration of GABAmide so as to establish a nexus between the therapeutic result and the administered compound. Beyond satisfying the test laid out in *In re Magerlein*, in regard to the pending claims we are able to go further and identify the cause of the side effects in progabide namely, the 4-chlorophenyl-5-fluoro-2-hydroxyphenylmethanone byproduct.

Bergmann states on page 15, para. 4: "There is substantial evidence from these and other binding studies that progabide and SL75012 act like GABA at all known GABA receptor binding sites (7, 8)." GABAmide is conspicuously absent from this grouping. This statement can be interpreted to mean that GABAmide does not act like GABA at all known GABA receptor

binding sites or alternatively, that GABAmide was considered too unstable to properly test. Regardless of the interpretation, applicant submits that the claimed subject matter would not be obvious to one of skill in the art upon reading either Aebisher et al. or Bergmann, each alone or in combination.

Based on the existing case law, and the fact that the prior art fails to appreciate that the side effects associated with progabide as a GABA mimetic derive from halogenated aromatic rings thereof and that GABAmide is stable enough for intrathecal or intraventricular delivery, it is respectfully submitted that the pending claims, all recited administration of GABAmide are non-obvious over the prior art. Reconsideration and withdrawal of the outstanding rejections under 35 U.S.C. §103(a) is requested.

Summary

Claims 1-3, 5-13, 15-18 and 26 are pending in the present application. Claims 1, 11, 18 and 26 are the only claims in independent form. Applicant submits that the present claims are believed to be in condition for allowance. Therefore, allowance of the pending claims and the passing of this application to issuance are solicited. Should the Examiner have suggestions as to how to form of a pending claim may be improved, she is respectfully requested to contact the undersigned attorney to resolve any remaining issues.

Respectfully submitted,

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